

Appl. No. 10/726,134

Amdt. dated March 21, 2006

Reply to Office action of September 21, 2005

IN THE SPECIFICATION:

On page 3, beginning on line 20 replace paragraph [0012] with the following paragraph:

[0012] In one embodiment, the present invention provides a device for the detection of ligands comprising ~~at least one~~ a plurality of substantially spherical substrates or particles; at least one receptor attached to said the spherical particles substrate, wherein said at least one receptor is capable of binding to a ligand to form a receptor-ligand complex and wherein the formation of said receptor-ligand complex produces a signal; and an amplification mechanism comprising a liquid crystalline material, wherein said amplification mechanism amplifies said signal upon receptor-ligand complex formation.

On page 3, beginning on line 28 and continuing on page 4 replace paragraph [0013] with the following paragraph:

[0013] In another embodiment, the present invention also provides a method for detecting ligands comprising providing a device capable of detecting ligands, said device comprising a plurality of ~~at least one~~ substantially spherical particles or substrates, at least one receptor attached to the said spherical particles substrate, wherein said at least one receptor is capable of binding to a ligand to form a receptor-ligand complex and wherein the formation of said receptor-ligand complex produces a signal; and an amplification mechanism comprising a liquid crystalline material, wherein said amplification mechanism comprises a liquid crystalline material and amplifies said signal upon receptor-ligand complex formation; exposing a sample containing at least one ligand to at least one substrate; allowing said receptor to interact with said at least one ligand to form at least one receptor-ligand complex, and measuring the signal generated by said receptor-ligand complex formation.

On page 6, beginning on line 25 replace paragraph [0023] with the following paragraph:

[0023] FIG. 2A is a representation of a non-porous (solid) spherical particle or substrate having a plurality of receptors attached to the outer surface of the sphere.

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On page 6, beginning on line 28 replace paragraph [0024] with the following paragraph:
[0024] FIG. 2B is a representation of a porous spherical particle or substrate having a plurality of receptors attached to the outer surface of the sphere and within the pores of the sphere.

On page 7, beginning on line 1 replace paragraph [0025] with the following paragraph:
[0025] FIG. 2C is a representation of a non-porous (solid) spherical particle or substrate having a plurality of receptors attached to the outer surface of the sphere with ligand bound to a portion of the receptors.

On page 7, beginning on line 5 replace paragraph [0026] with the following paragraph:
[0026] FIG. 2D is a representation of a porous spherical particle or substrate having a plurality of receptors attached to the outer surface of the sphere and within the pores of the sphere with ligand bound to a portion of the receptors.

On page 7, beginning on line 9 replace paragraph [0027] with the following paragraph:
[0027] FIG. 3A is a representation of, a non-porous (solid) spherical particle or substrate having a plurality of receptors attached to the outer surface of the sphere showing the liquid crystalline material orientation about the receptor-bound sphere.

On page 7, beginning on line 13 replace paragraph [0028] with the following paragraph:
[0028] FIG. 3B is a representation of, a porous spherical particle or substrate having a plurality of receptors attached to the outer surface of the sphere and within the pores of the sphere showing the liquid crystalline material orientation about the receptor-bound sphere.

On page 7, beginning on line 19 replace paragraph [0029] with the following paragraph:
[0029] FIG. 3C is a representation of a non-porous (solid) spherical particle or substrate having a plurality of receptors attached to the outer surface of the sphere with ligand bound to a portion of the receptors showing the change in liquid crystalline material orientation about the sphere when ligand is bound.

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On page 7, beginning on line 23 replace paragraph [0030] with the following paragraph:
[0030] FIG. 3D is a representation of a porous spherical particle or substrate having a plurality of receptors attached to the outer surface of the sphere and within the pores of the sphere with ligand bound to a portion of the receptors showing the change in liquid crystalline material orientation about the sphere when ligand is bound.

On page 20, beginning on line 1 replace paragraph [0066] with the following paragraph:
[0066] In one preferred embodiment, the device of the present invention may include ~~at least one~~ a plurality of substantially spherical particles or substrates to which receptors may be attached. The receptor or receptors that are attached to the spherical particles ~~substrate~~ must be capable of binding to a desired ligand to form a receptor-ligand complex such that, upon formation of said receptor-ligand complex a signal is produced. An amplification mechanism is interfaced with the receptor-ligand complex, where the amplification mechanism amplifies the signal produced by receptor-ligand complex formation.

On page 20, beginning on line 10 replace paragraph [0067] with the following paragraph:
[0067] ~~The substantially spherical substrate~~ particles utilized in the present invention can be non-porous (solid) or porous. In one embodiment, the substantially spherical substrate is a solid sphere and the at least one receptor is attached to the outer surface of the spherical ~~substrate~~ particles.

On page 20, beginning on line 15 replace paragraph [0068] with the following paragraph:
[0068] In another embodiment, the ~~substantially spherical substrate~~ particles are is porous. According to this embodiment, the at least one receptor may be attached to either the surface of ~~said porous substantially spherical substrate~~ the particle, the pores of said the porous ~~substantially spherical particles~~ substrate, or both. By way of non-limiting example, if only one receptor is attached to the ~~substantially spherical substrate~~ particle, then the receptor can be attached to either the outer surface of the porous sphere or in the pores of the sphere. In embodiment having more than one receptor attached to the ~~spherical substrate~~ particle, then the receptors can all be attached to the outer surface of the sphere, all the receptor can be attached within the pores of the sphere, or some receptors can be attached to the outer surface of the

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sphere and other receptors can be attached to the pores of the sphere. The use of a particle such as a porous sphere or bead provides a greater surface area on which to attach receptors and, therefore, would also permit surface and luminal receptor-ligand interactions.

On page 20, beginning on line 29 replace paragraph [0069] with the following paragraph:
[0069] The receptors may be attached to the ~~spherical-substrate~~ particle in any manner known in the art, including chemical attachment and physical attachment. In one preferred embodiment, the receptors are attached to the ~~spherical-substrate~~ particle by a chemical attachment, such as by covalent bonding to sulfate, amine, carboxyl or hydroxyl groups imbedded in the ~~spherical-substrate~~ particle. However, it should be noted that the receptors wherein said at least one receptor is attached to ~~said spherical-substrate~~ the particle by any means of physical attachment.

On page 21, beginning on line 5 replace paragraph [0070] with the following paragraph:
[0070] The ~~substantially receptor-coated spherical-substrate~~ particles may be is made from a material including, but not limited to, polymeric and inorganic materials. In one preferred embodiment, the substantially receptor-coated spherical substrate is comprised of a polymeric material. Suitable polymeric materials which may comprise the spherical substrate include, but are not limited to, polyalkenes, polyacrylates, polymethacrylates, polyvinyls, polystyrenes, polycarbonates, polyesters, polyurethanes, polyamides, polyimides, polysulfones, polysiloxanes, polysilanes, polyethers, polycations, polyanions, and polycarboxylates. One particularly useful polymeric material used to manufacture the spherical substrate is polystyrene, especially when modified with copolymers of acrylic ester, chloromethylstyrene, methylolamine, methyl methacrylate or made zwitterionic. If a polycation is utilized as the material of the spherical substrate, one particularly suitable polycation is poly(diallyldimethylammoniumchloride).

On page 21, beginning on line 19 replace paragraph [0071] with the following paragraph:
[0071] In another embodiment, the ~~substantially receptor-coated spherical-substrate is~~ particles may be made from an inorganic material. Suitable inorganic materials include, but are not limited to, glass, silicon, and colloidal gold. In one preferred embodiment, the spherical substrate is a glass bead.

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On page 21, beginning on line 24 replace paragraph [0072] with the following paragraph:
[0072] The liquid crystalline material that is utilized with the ~~substantially-coated-spherical-substrate~~ particles includes all known types of thermotropic liquid crystalline materials and lyotropic liquid crystalline materials. In one preferred embodiment, lyotropic liquid crystalline material is used as the amplification mechanism. In another embodiment, lyotropic liquid crystalline materials of different origin, including surfactant and lyotropic chromonic liquid crystalline material, may used with the spherical ~~substrate~~ particles.

On page 22, beginning on line 7 replace paragraph [0074] with the following paragraph:
[0074] In another embodiment, the present invention provides a method for detecting ligands. The method for detecting ligands, according this embodiment, includes providing a device that comprises ~~at least one substantially-spherical-substrate~~ a plurality of particles, at least one receptor attached to each of the plurality of particles ~~said-spherical-substrate~~, and an amplification mechanism. The at least one receptor must be capable of binding to a ligand to form a receptor-ligand complex and, upon formation of the receptor-ligand complex, a signal is produced. The amplification mechanism must be capable of amplifying the signal produced by the receptor-ligand complex formation. Generally, a sample containing ligands specific to the receptor that is attached to the particles ~~sphere~~ is exposed to the device. After exposing the ligand-containing sample to the device, the receptor or plurality of receptors that are attached to each of the plurality of particles ~~sphere~~ are allowed to interact with the ligands in the sample to form at least one receptor-ligand complex. The formation of the receptor-ligand complex produces a detectable signal. The signal generated by the formation of the receptor-ligand complex is amplified by the amplification mechanism, namely, the liquid crystalline material. The amplified signal may then be measured and quantitated by those known methods easily determined by those having ordinary skill in the art.

On page 22, beginning on line 25 replace paragraph [0076] with the following paragraph:
[0076] In another embodiment, the device for the detection of ligands comprises ~~at least one a~~ plurality of particles or substantially-spherical substrates coated with a receptor-binding or receptor-crosslinking material, at least one receptor attached to the coated ~~spherical-substrate~~ particle, and an amplification mechanism comprising a liquid crystalline material. The at least

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one receptor is capable of binding to a ligand to form a receptor-ligand complex and the formation of the receptor-ligand complex produces a signal. The signal produced is then amplified by the amplification mechanism upon receptor-ligand complex formation. According to the present embodiment, the crosslinker material may be, without limitation, natural or synthetic polymers, proteins, and secondary antibodies.

On page 23, beginning on line 15 replace paragraph [0077] with the following paragraph:
[0077] In one preferred embodiment, molecules with specificity for receptors, such as the specificity exhibited by Protein A, Protein G or anti-immunoglobulin antibodies for immunoglobulins, will be chemically cross linked to the spherical substrate particles. Receptors with specificity for unique pathogens, toxins or proteins will then be bound to the immobilized molecules.

On page 23, beginning on line 21 replace paragraph [0078] with the following paragraph:
[0078] In another embodiment, the present invention provides a method for detecting ligands comprising providing a device capable of detecting ligands. According to this embodiment, the device comprises a plurality of particles ~~at least one substantially spherical substrate~~ coated with a receptor-binding material; at least one receptor attached to the particles ~~said spherical substrate~~, and an amplification mechanism comprising a liquid crystalline material. The at least one receptor is capable of binding to a ligand to form a receptor-ligand complex and upon the formation of a receptor-ligand complex produces a signal. The amplification mechanism amplifies said signal upon receptor-ligand complex formation. The method includes exposing a sample containing at least one ligand to at least one of said substrate and allowing the receptor to interact with the ligands in the sample to form at least one receptor-ligand complex. The signal produced by said receptor-ligand complex formation is then measured.